heterologous insert which is also a locking sequence that prevents DNA rotation. Figure 2E depicts a heterologous insert which forms a triplex with a secondary probe, thereby forming a locking sequence that prevents DNA rotation. Figure 2F depicts a double D-loop in which the internal homology clamp or anchoring sequence is formed from the target sequences, i.e. wherein the targeting polynucleotides are shorter than the target sequence.

Please replace the paragraph beginning at page 6, line 1, with the following rewritten paragraph:

Figure 9C depicts DNA probe oligonucleotides QI_W (SEQ ID NO:5) and QI_C (SEQ ID NO:6) (Quadruple DNA-forming insert) contains the heterologous insert sequence$T_2G_4T_2G_4T_2$. (SEQ ID NO:9) "b": biotin.

Please replace the paragraph beginning at page 11, line 4, with the following rewritten paragraph:

The crystal structure of RecA protein in the absence of DNA reveals two disordered polypeptide loops, L1 and L2, that are proposed nucleic acid binding sites (Story et al, Nature 355(6358):318-325 (1992)). Several lines of evidence indicate that loop L2 is the oligonucleotide binding domain: a) proteolysis of ssDNA-RecA complexes yields a unique 4-kD peptide protected by the DNA that spans this loop (Gardner et al., Eur J. Biochem. 233:419-425 (1995)); b) crosslinks between a ssDNA and RecA map to loops L1 and L2; c) the intrinsic fluoresescence of peptides in loop2 is quenched in RecA-DNA complexes; and d) the 20 amino acid FECO peptide corresponding to the L2 polypeptide loop (NQIRMKIGVMFGNPETTTGG) (SEQ ID NO:12) binds to ssDNA.

Please replace the paragraph beginning at page 12, line 1, with the following rewritten paragraph:

Accordingly, in one embodiment, FECO oligopeptide (NQIRMKIGVMFGNPETTTGG) (SEQ ID NO:12) and NLS-FECO (PLLLALVNQIRMKIGVMFGNPETTTGG) (SEQ ID NO:13) are used to for

specific gene targeting and by locked D-loop hybrids. E. coli RecA protein does not contain a eukaryotic cell nuclear localization signal (NLS) facilitating the transport of exogenously added proteins to the nucleus. Certain oligopeptides and proteins that do not have the NLS signal are not actively transported into the nucleus. For example, it has been shown by immunofluorescence staining that when wild type RecA protein is microinjected into the cytoplasm of certain human cells, it remains in the cytoplasm and it does not significantly enter the nucleus (Kido et al., Exp. Cell Res. 198:107-114 (1992)). In eukaryotic cells, nuclear proteins are initially synthesized in the cytoplasm and then are rapidly transported into the nucleus. The precise mechanism of nuclear transport is not fully known, and active transport has been suggested (Yamaizumi et al., Nature 273:782-784 (1978); Sugawa et al., Exp. cell Res. 159:419-429 (1985)); Tsuneoka et al., J. Biol. Chem. 261:1829-1834 (1986); Imamoto-Sonobe et al., Proc. Natl. Acad. Sci. USA 85:3426-3430 (1988)). Kalderon et al., Nature 311:5981 (1984a); Kalderon et al. Cell 3:499-509 (1984b)). Kalderon et al., (1984a, b), showed that a short oligopeptide sequence of the SV40 virus large T-antigen, PLLLALV (SEQ ID NO:14), specifies a nuclear localization signal (NLS) (Kalderon et al., 1984a and 1984b). Fusion of exogenous proteins with this viral NLS peptide has also been shown to direct the transport of fused exogenous proteins into the nucleus. For example, when this viral NLS peptide was fused to the RecA protein and injected into the cytoplasm, the PLLLALV (SEQ ID NO:14) modified RecA protein was efficiently transported to the nucleus (Kido et al., 1992). More importantly, the NLS fused RecA protein retains its full in vivo RecA activity.

Please replace the paragraph beginning at page 12, line 37, with the following rewritten paragraph:

In a preferred embodiment, the 20 amino acid FECO peptide (NQIRMKIGVMFGNPETTTGG) (SEQ ID NO:12) and FECO with a NLS (PLLLALVNQIRMKIGVMFGNPETTTGG) (SEQ ID NO:13) attached to the N-terminal end are used for cssDNA targeting to a homology clamped site in the duplex DNA.

Please replace the paragraph beginning at page 14, line 28, with the following rewritten paragraph:

B6

Targeting polynucleotides have a number of relevant structures. In a preferred embodiment, the target polynucleotides comprise homology clamps, i.e. sequences that substantially correspond to, or are substantially complementary to, a predetermined endogenous DNA sequence. The term "corresponds to" is used herein to mean that a polynucleotide sequence is homologous (i.e., may be similar or identical, not strictly evolutionarily related) to all or a portion of a reference polynucleotide sequence, or that a polynucleotide sequence is identical to a reference polynucleotide sequence. In contradistinction, the term "complementary to" is used herein to mean that the complementary sequence is homologous to all or a portion of a reference polynucleotide sequence. As outlined below, preferably, the homology is at least 70%, preferably 85%, and more preferably 95% identical. Thus, the complementarity between two single-stranded targeting polynucleotides need not be perfect. For illustration, the nucleotide sequence "TATAC" (SEQ ID NO:15) corresponds to or is identical to a reference sequence "TATAC" (SEQ ID NO:15) and is perfectly complementary to a reference sequence "GTATA" (SEQ ID NO:16).

Please replace the paragraph beginning at page 38, line 25, with the following rewritten paragraph:

B7

Three sets of complementary single stranded (css) probes were designed as follows. The target sequence was the 62 nucleotides from bases 667 to 723 of pBluescript II SK(−) (Stratagene. LaJolla, CA; Figure 9A). The control reaction comprises two complementary single stranded nucleic acids (cssDNA) comprising these 62 bases and their complement. Targeting polynucleotides comprising the quadruplex forming lock 5-TTGGGGTTGGGGTT (SEQ ID NO:9) are shown in Figure 9C (Sundquist et al., (1989)). Targeting polynucleotides also were made comprising the triplex forming lock GGGTGGTGGGTGGGGTATTAGGGGAGGGAGGAGGG (SEQ ID NO:17) inserted in the sequence (Dayn et al., PNAS USA 89:11406 (1992)).

Please replace the paragraph beginning at page 45, line 16, with the following rewritten paragraph:

In these experiments a modified version of *in vitro* transcription assay described by Golub *et al.*, (1992, 1993, *supra*) was used. Briefly, double-stranded DNA fragments having about 300 bp of homology (including T7 promoter) with pBluescript II SK(-) were obtained by PCR either from pBluescript II SK(-) or pTL plasmid (pTL plasmid was derived from pBluescript II SK(-) by inserting the triplex forming sequence, 5-GGGTGGTGGGTGGGGTATTAGGGGAGGGGAGGAGG-3 (SEQ ID NO:17) (Dayn *et al.*, 1992, *supra*) into the *Hin*dIII/*Eco*RI site; Figure 16). The probes obtained from pTL plasmid were designed to form a triplex lock when targeted to pBluescript II SK(-). In addition, probes shown in Figure 9A-C (SEQ ID NO:1-6) also are used.

On page 70, immediately preceding the claims, please insert the enclosed text entitled "SEQUENCE LISTING".

In The Claims:

Please cancel Claims 6, 27, and 48 without prejudice to Applicants' rights to pursue the subject matter of these claims in one or more divisional, continuation, or continuation-in-part applications.

Please amend the claims as follows:

1. (Amended) A composition comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each comprising:

a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequence; and

b) at least one locking sequence.

2. (Amended) The composition of claim 1 further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said locking sequences.